

WHAT IS CLAIMED IS:

1. A compound comprising:

i) 1-10 targeting moieties;

ii) a chelator; and

iii) 0-1 linking groups between the targeting moiety and chelator;

wherein the targeting moiety is a matrix metalloproteinase inhibitor; and

wherein the chelator is capable of conjugating to a cytotoxic radioisotope.

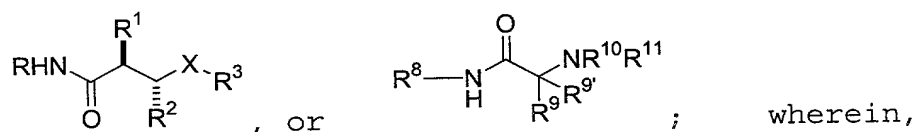
2. A compound according to claim 1, wherein the targeting moiety is a matrix metalloproteinase inhibitor having an inhibitory constant K_i of <1000 nM.

3. A compound according to claim 1, wherein the targeting moiety is a matrix metalloproteinase inhibitor having an inhibitory constant K_i of <100 nM.

4. A compound according to claim 1, comprising 1-5 targeting moieties.

5. A compound according to claim 1, comprising one targeting moiety.

6. A compound according to claim 1, wherein the targeting moiety is a matrix metalloproteinase inhibitor of the formulae (Ia) or (Ib):

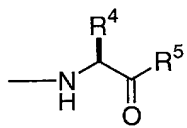


R is independently OH or $-\text{CH}_2\text{SH}$;

R¹ is independently selected at each occurrence from the group:
H, OH, C₁₋₃ alkyl, C₂₋₃ alkenyl, C₂₋₃ alkynyl, and
heterocycle-S-CH₂-;

R² is independently C₁₋₂₀ alkyl;

X is independently C=O or SO₂, provided when X is C=O, R³ is



, and when X is SO₂, R³ is independently selected
from the group: aryl substituted with 0-2 R⁶, and
heterocycle substituted with 0-2 R⁶;

R⁴ is independently selected at each occurrence from the group:
C₁₋₆ alkyl, phenyl, and benzyl;

R⁵ is independently at each occurrence from the group: NH(C₁₋₆
alkyl), NH-phenyl, and NH-heterocycle; wherein said alkyl,
phenyl and heterocycle groups are optionally substituted
with a bond to the linking group or a bond to the chelator;

R⁶ is independently aryloxy substituted with 0-3 R⁷;

R⁷ is independently halogen or methoxy;

or alternatively,

R¹ and R⁴ may be taken together to form a bridging group of the
formula -(CH₂)₃-O-phenyl-CH₂-, optionally substituted with a
bond to the linking group or a bond to the chelator;

or alternatively,

R¹ and R² may be taken together to form a bridging group of the formula $-(CH_2)_3-NH-$, optionally substituted with a bond to the linking group or a bond to the chelator; or

R¹ and R² taken together with the nitrogen and carbon atom through which they are attached form a C₅₋₇ atom saturated ring system substituted with one or more substituents selected from the group consisting of: a bond to Ln, a bond to Ch, and $-C(=O)-NR^{29}R^{30}$;

R⁸ is independently at each occurrence OH or phenyl, optionally substituted with a bond to the linking group or a bond to the chelator, provided that when R⁸ is phenyl, R¹⁰ is $-C(=O)-CR^{12}-NH-CH(CH_3)-COOH$;

R⁹ and R^{9'} are independently H, C₁₋₆ alkyl optionally substituted with a bond to the linking group or a bond to the chelator, or are taken together with the carbon atom to which R⁹ and R^{9'} are attached to form a 5-7 atom saturated, partially unsaturated or aromatic ring system containing 0-3 heteroatoms selected from O, N, SO₂ and S, said ring system substituted with R⁶ and optionally substituted with a bond to the linking group or a bond to the chelator;

R¹⁰ and R¹¹ are independently H, or C₁₋₆ alkyl optionally substituted with a bond to the linking group or a bond to the chelator, or are taken together with the nitrogen atom to which they are attached to form a 5-7 atom saturated, partially unsaturated or aromatic ring system containing 0-3 heteroatoms selected from O, N, SO₂ and S, said ring system optionally substituted with 0-3 R²⁷, a bond to the linking group or a bond to the chelator;

or alternatively,

R⁹ and R¹⁰ are taken together with the carbon atom to which they are attached to form a 5-7 atom saturated, partially unsaturated or aromatic ring system containing 0-3 heteroatoms selected from O, N, SO₂ and S, said ring system optionally substituted with a bond to the linking group or a bond to the chelator; and

R¹² is independently C₁₋₂₀ alkyl;

R²⁷ is =O, C₁₋₄ alkyl, or phenyl substituted with R²⁸;

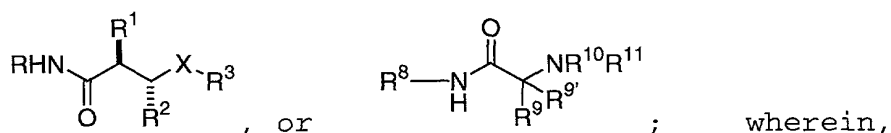
R²⁸ is a phenoxy group substituted with 0-2 OCH₃ groups;

R²⁹ and R³⁰ taken together with the nitrogen atom through which they are attached form a C₅₋₇ atom saturated ring system substituted with R³¹; and

R³¹ is a benzyloxy group substituted with C₁₋₄ alkyl.

7. A compound according to claim 1 wherein

A compound according to claim 1, wherein the targeting moiety is a matrix metalloproteinase inhibitor of the formulae (Ia) or (Ib):



R is OH;

R¹ is independently selected at each occurrence from the group:
H, OH, C₁₋₃ alkyl, C₂₋₃ alkenyl, C₂₋₃ alkynyl, and
heterocycle-S-CH₂-;

R² is independently C₁₋₆ alkyl;

X is C=O;

R⁴ is independently selected at each occurrence from the group:
C₁₋₆ alkyl, phenyl, and benzyl;

R⁵ is independently at each occurrence from the group: NH(C₁₋₆ alkyl), NH-phenyl, and NH-heterocycle; wherein said alkyl, phenyl and heterocycle groups are optionally substituted with a bond to the linking group or a bond to the chelator;

R⁶ is independently aryloxy substituted with 0-3 R⁷;

R⁷ is independently halogen or methoxy;

or alternatively,

R¹ and R⁴ may be taken together to form a bridging group of the formula $-(CH_2)_3-O-phenyl-CH_2-$, optionally substituted with a bond to the linking group or a bond to the chelator;

or alternatively,

R¹ and R² may be taken together to form a bridging group of the formula $-(CH_2)_3-NH-$, optionally substituted with a bond to the linking group or a bond to the chelator; or

R¹ and R² taken together with the nitrogen and carbon atom through which they are attached form a C₅₋₇ atom saturated ring system substituted with one or more substituents selected from the group consisting of: a bond to Ln, a bond to Ch, and $-C(=O)-NR^{29}R^{30}$;

R⁸ is OH;

R⁹ and R^{9'} are independently H, C₁₋₆ alkyl optionally substituted with a bond to the linking group or a bond to the chelator, or are taken together with the carbon atom to which R⁹ and R^{9'} are attached to form a 5-7 atom saturated, partially unsaturated or aromatic ring system containing 0-1 heteroatoms selected from O, N, , said ring system optionally substituted with a bond to the linking group or a bond to the chelator;

R¹⁰ and R¹¹ are independently H, or C₁₋₆ alkyl optionally substituted with a bond to the linking group or a bond to the chelator, or are taken together with the nitrogen atom to which they are attached to form a 5-7 atom saturated, partially unsaturated or aromatic ring system containing 0-1 heteroatoms selected from O, N, , said ring system optionally substituted with 0-3 R²⁷, a bond to the linking group or a bond to the chelator;

or alternatively,

R⁹ and R¹⁰ are taken together with the carbon atom to which they are attached to form a 5-7 atom saturated, partially unsaturated or aromatic ring system containing 0-1 heteroatoms selected from O, N, , said ring system optionally substituted with a bond to the linking group or a bond to the chelator; and

R¹² is independently C₁₋₆ alkyl;

R²⁷ is =O, C₁₋₄ alkyl, or phenyl substituted with R²⁸;

R²⁸ is a phenoxy group substituted with 0-2 OCH₃ groups;

R²⁹ and R³⁰ taken together with the nitrogen atom through which they are attached form a C₅₋₇ atom saturated ring system substituted with R³¹; and

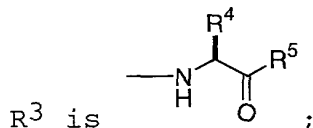
R³¹ is a benzyloxy group substituted with C₁₋₄ alkyl.

8. A compound according to claim 7 wherein:

R is -OH;

R² is C₁₋₆ alkyl;

X is C=O;



R¹ and R⁴ are taken together to form a bridging group of formula
-(CH₂)₃-O-phenyl-CH₂-;

R⁵ is NH(C₁₋₆alkyl), substituted with a bond to the linking group or a bond to the chelator.

A compound according to claim 14, wherein:

R is -OH;

R⁹ is C₁ alkyl substituted with a bond to Ln;

R¹⁰ and R¹¹ taken together with the nitrogen atom to which they are attached form a 5 atom saturated ring system, said ring system is substituted with 0-3 R²⁷;

R²⁷ is =O, C₁₋₄ alkyl, or phenyl substituted with R²⁸; and

R²⁸ is a phenoxy group substituted with 0-2 OCH₃ groups.

9. A compound according to claim 7, wherein:

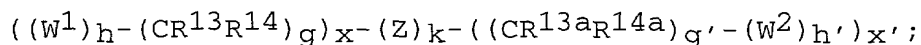
R is -OH;

R¹ and R² taken together with the nitrogen and carbon atom through which they are attached form a C₅₋₇ atom saturated ring system substituted with one or more substituents selected from the group consisting of: a bond to Ln, a bond to Ch, and -C(=O)-NR²⁹R³⁰;

R²⁹ and R³⁰ taken together with the nitrogen atom through which they are attached form a C₅₋₇ atom saturated ring system substituted with R³¹; and

R³¹ is a benzyloxy group substituted with C₁₋₄ alkyl.

10. A compound according to claim 1, wherein the linking group is of the formula:



W^1 and W^2 are independently selected at each occurrence from the group: O, S, NH, NHC(=O), C(=O)NH, $NR^{15}C(=O)$, C(=O) NR^{15} , C(=O), C(=O)O, OC(=O), NHC(=S)NH, NHC(=O)NH, SO₂, SO₂NH, - (OCH₂CH₂)₇₆₋₈₄, (OCH₂CH₂)_s, (CH₂CH₂O)_{s'}, (OCH₂CH₂CH₂)_{s''}, (CH₂CH₂CH₂O)_t, and (aa)_{t'};

aa is independently at each occurrence an amino acid;

Z is selected from the group: aryl substituted with 0-3 R^{16} , C₃-10 cycloalkyl substituted with 0-3 R^{16} , and a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-3 R^{16} ;

R^{13} , R^{13a} , R^{14} , R^{14a} , and R^{15} are independently selected at each occurrence from the group: H, =O, COOH, SO₃H, PO₃H, C₁-C₅ alkyl substituted with 0-3 R^{16} , aryl substituted with 0-3 R^{16} , benzyl substituted with 0-3 R^{16} , and C₁-C₅ alkoxy substituted with 0-3 R^{16} , NHC(=O) R^{17} , C(=O)NHR¹⁷, NHC(=O)NHR¹⁷, NHR¹⁷, R^{17} , and a bond to the chelator;

R^{16} is independently selected at each occurrence from the group: a bond to the chelator, COOR¹⁷, C(=O)NHR¹⁷, NHC(=O) R^{17} , OH, NHR¹⁷, SO₃H, PO₃H, -OPO₃H₂, -OSO₃H, aryl substituted with 0-3 R^{17} , C₁-5 alkyl substituted with 0-1 R^{18} , C₁-5 alkoxy substituted with 0-1 R^{18} , and a 5-10 membered heterocyclic

ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-3 R¹⁷;

R¹⁷ is independently selected at each occurrence from the group:

H, alkyl substituted with 0-1 R¹⁸, aryl substituted with 0-1 R¹⁸, a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-1 R¹⁸, C₃₋₁₀ cycloalkyl substituted with 0-1 R¹⁸, polyalkylene glycol substituted with 0-1 R¹⁸, carbohydrate substituted with 0-1 R¹⁸, cyclodextrin substituted with 0-1 R¹⁸, amino acid substituted with 0-1 R¹⁸, polycarboxyalkyl substituted with 0-1 R¹⁸, polyazaalkyl substituted with 0-1 R¹⁸, peptide substituted with 0-1 R¹⁸, wherein the peptide is comprised of 2-10 amino acids, 3,6-O-disulfo-B-D-galactopyranosyl, bis(phosphonomethyl)glycine, and a bond to the chelator;

R¹⁸ is a bond to the chelator;

k is selected from 0, 1, and 2;

h is selected from 0, 1, and 2;

h' is selected from 0, 1, and 2;

g is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;

g' is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;

s is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;

s' is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;

s" is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;

t is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;

t' is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;

x is selected from 0, 1, 2, 3, 4, and 5; and

x' is selected from 0, 1, 2, 3, 4, and 5.

11. A compound according to claim 10 wherein

W¹ and W² are independently selected at each occurrence from the group: O, NH, NHC(=O), C(=O)NH, NR¹⁵C(=O), C(=O)NR¹⁵, C(=O), C(=O)O, OC(=O), NHC(=S)NH, NHC(=O)NH, SO₂, - (CH₂CH₂O)₇₆₋₈₄-, (OCH₂CH₂)_s, (CH₂CH₂O)_{s'}, (OCH₂CH₂CH₂)_{s''}, (CH₂CH₂CH₂O)_t, and (aa)_{t'};

aa is independently at each occurrence an amino acid;

Z is selected from the group: aryl substituted with 0-1 R¹⁶, C₃-10 cycloalkyl substituted with 0-1 R¹⁶, and a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-1 R¹⁶;

R¹³, R^{13a}, R¹⁴, R^{14a}, and R¹⁵ are independently selected at each occurrence from the group: H, =O, COOH, SO₃H, C₁-C₅ alkyl substituted with 0-1 R¹⁶, aryl substituted with 0-1 R¹⁶, benzyl substituted with 0-1 R¹⁶, and C₁-C₅ alkoxy substituted with 0-1 R¹⁶, NHC(=O)R¹⁷, C(=O)NHR¹⁷, NHC(=O)NHR¹⁷, NHR¹⁷, R¹⁷, and a bond to the chelator;

k is 0 or 1;

s is selected from 0, 1, 2, 3, 4, and 5;

s' is selected from 0, 1, 2, 3, 4, and 5;

s'' is selected from 0, 1, 2, 3, 4, and 5; and

t is selected from 0, 1, 2, 3, 4, and 5.

12. A compound according to claim 10, wherein:

W¹ is C(=O)NR¹⁵;

h is 1;

g is 3;

R¹³ and R¹⁴ are independently H;

x is 1;
k is 0;
g' is 0;
h' is 1;
W² is NH; and
x' is 1.

13. A compound according to claim 10, wherein:

x is 0;
k is 1;
Z is aryl substituted with 0-3 R¹⁶;
g' is 1;
W² is NH;
R^{13a} and R^{14a} are independently H;
h' is 1; and
x' is 1.

14. A compound according to claim 10, wherein:

W¹ is C(=O)NR¹⁵;
h is 1;
g is 2;
R¹³ and R¹⁴ are independently H;
x is 1;
k is 0;
g' is 1;
R^{13a} and R^{14a} are independently H; or C1-5 alkyl substituted
with 0-3 R¹⁶;
R¹⁶ is SO₃H;
W² is NHC(=O) or NH;
h' is 1; and
x' is 2.

15. A compound according to claim 10, wherein:

W¹ is C(=O)NH;

h is 1;
 g is 3;
 R^{13} and R^{14} are independently H;
 k is 0;
 g' is 0;
 x is 1;
 W^2 is $-NH(C=O)-$ or $-(OCH_2CH_2)_{76-84}-$;
 h' is 2; and
 x' is 1.

16. A compound according to claim 10, wherein:
 x is 0;
 k is 0;
 g' is 3;
 h' is 1;
 W^2 is NH; and
 x' is 1.

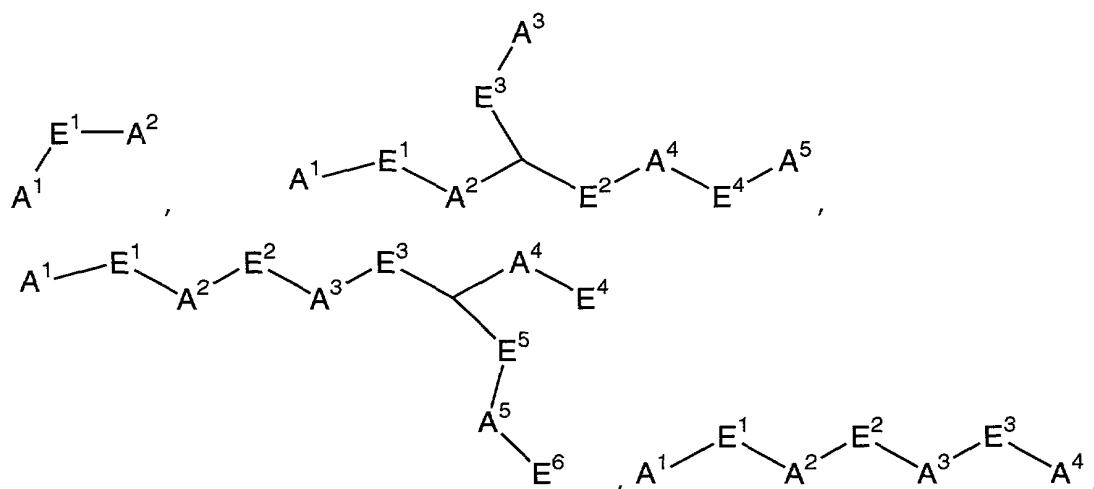
17. A compound according to claim 10, wherein:
 x is 0;
 Z is aryl substituted with 0-3 R^{16} ;
 k is 1;
 g' is 1;
 R^{13} and R^{14a} are independently H;
 W^2 is $NHC(=O)$ or $-(OCH_2CH_2)_{76-84}-$; and
 x' is 1.

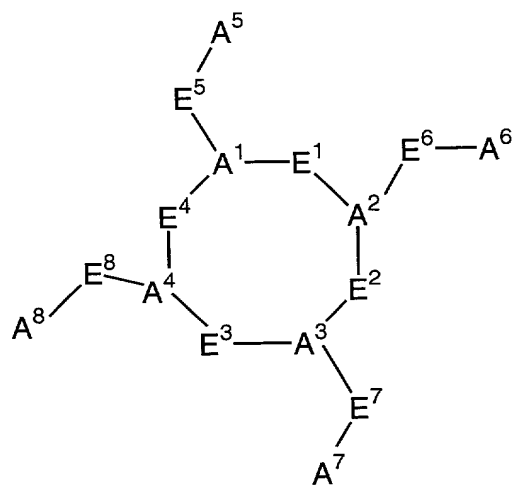
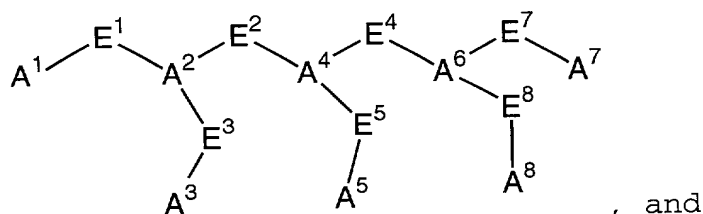
18. A compound according to claim 10, wherein:
 W^1 is $C=O$;
 g is 2;
 R^{13} and R^{14} are independently H;
 k is 0;
 g' is 0;
 h' is 1;

W^2 is NH; and
 x' is 1.

19. A compound according to claim 1 wherein the linking group is absent.

20. A compound according to claim 1, wherein the chelator is a metal bonding unit having a formula selected from the group:





A¹, A², A³, A⁴, A⁵, A⁶, A⁷, and A⁸ are independently selected at each occurrence from the group: N, NR²⁶, NR¹⁹, NR¹⁹R²⁰, S, SH, -S(Pg), O, OH, PR¹⁹, PR¹⁹R²⁰, -O-P(O)(R²¹)-O-, P(O)R²¹R²², a bond to the targeting moiety and a bond to the linking group;

Pg is a thiol protecting group;

E¹, E², E³, E⁴, E⁵, E⁶, E⁷, and E⁸ are independently a bond, CH, or a spacer group independently selected at each occurrence from the group: C₁-C₁₆ alkyl substituted with 0-3 R²³, aryl substituted with 0-3 R²³, C₃-10 cycloalkyl substituted with 0-3 R²³, heterocyclo-C₁-10 alkyl substituted with 0-3 R²³, wherein the heterocyclo group is a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O, C₆-10 aryl-C₁-10 alkyl substituted with 0-3 R²³, C₁-10 alkyl-C₆-10 aryl-substituted with 0-3 R²³, and a 5-10 membered heterocyclic

ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-3 R²³;

R¹⁹ and R²⁰ are each independently selected from the group: a bond to the linking group, a bond to the targeting moiety, hydrogen, C₁-C₁₀ alkyl substituted with 0-3 R²³, aryl substituted with 0-3 R²³, C₁-₁₀ cycloalkyl substituted with 0-3 R²³, heterocyclo-C₁-₁₀ alkyl substituted with 0-3 R²³, wherein the heterocyclo group is a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O, C₆-₁₀ aryl-C₁-₁₀ alkyl substituted with 0-3 R²³, C₁-₁₀ alkyl-C₆-₁₀ aryl-substituted with 0-3 R²³, a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-3 R²³, and an electron, provided that when one of R¹⁹ or R²⁰ is an electron, then the other is also an electron;

R²¹ and R²² are each independently selected from the group: a bond to the linking group, a bond to the targeting moiety, -OH, C₁-C₁₀ alkyl substituted with 0-3 R²³, C₁-C₁₀ alkyl substituted with 0-3 R²³, aryl substituted with 0-3 R²³, C₃-₁₀ cycloalkyl substituted with 0-3 R²³, heterocyclo-C₁-₁₀ alkyl substituted with 0-3 R²³, wherein the heterocyclo group is a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O, C₆-₁₀ aryl-C₁-₁₀ alkyl substituted with 0-3 R²³, C₁-₁₀ alkyl-C₆-₁₀ aryl-substituted with 0-3 R²³, and a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-3 R²³;

R²³ is independently selected at each occurrence from the group:
 a bond to the linking group, a bond to the targeting moiety, =O, F, Cl, Br, I, -CF₃, -CN, -CO₂R²⁴, -C(=O)R²⁴, -C(=O)N(R²⁴)₂, -CHO, -CH₂OR²⁴, -OC(=O)R²⁴, -OC(=O)OR^{24a}, -OR²⁴, -OC(=O)N(R²⁴)₂, -NR²⁵C(=O)R²⁴, -NR²⁵C(=O)OR^{24a}, -NR²⁵C(=O)N(R²⁴)₂, -NR²⁵SO₂N(R²⁴)₂, -NR²⁵SO₂R^{24a}, -SO₃H, -SO₂R^{24a}, -SR²⁴, -S(=O)R^{24a}, -SO₂N(R²⁴)₂, -N(R²⁴)₂, -NHC(=S)NHR²⁴, =NOR²⁴, NO₂, -C(=O)NHR²⁴, -C(=O)NHN(R²⁴)₂, -OCH₂CO₂H, 2-(1-morpholino)ethoxy, C₁-C₅ alkyl, C₂-C₄ alkenyl, C₃-C₆ cycloalkyl, C₃-C₆ cycloalkylmethyl, C₂-C₆ alkoxyalkyl, aryl substituted with 0-2 R²⁴, and a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O; and wherein at least one of A¹, A², A³, A⁴, A⁵, A⁶, A⁷, A⁸ or R²³ is a bond to the linking group or targeting moiety; R²⁴, R^{24a}, and R²⁵ are independently selected at each occurrence from the group: a bond to the linking group, a bond to the targeting moiety, H, C₁-C₆ alkyl, phenyl, benzyl, C₁-C₆ alkoxy, halide, nitro, cyano, and trifluoromethyl; and R²⁶ is a co-ordinate bond to a metal or a hydrazine protecting group.

21. A compound according to claim 20 wherein:

A¹, A², A³, A⁴, A⁵, A⁶, A⁷, and A⁸ are independently selected at each occurrence from the group: NR¹⁹, NR¹⁹R²⁰, S, SH, OH, a bond to the targeting moiety and a bond to the linking group;

E¹, E², E³, E⁴, E⁵, E⁶, E⁷, and E⁸ are independently a bond, CH, or a spacer group independently selected at each occurrence from the group: C₁-C₁₀ alkyl substituted with 0-3 R²³, aryl substituted with 0-3 R²³, C₃-10 cycloalkyl

substituted with 0-3 R^{23} , and a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-3 R^{23} ;

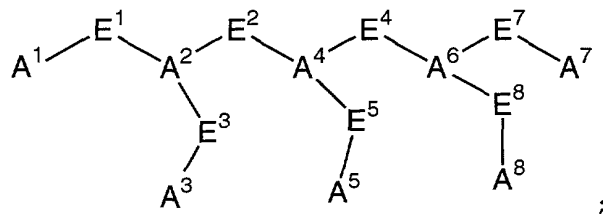
wherein at least one of A^1 , A^2 , A^3 , A^4 , A^5 , A^6 , A^7 , A^8 and R^{23} is a bond to the linking group or a targeting moiety;

R^{19} , and R^{20} are each independently selected from the group: a bond to the targeting moiety, a bond to the linking group, hydrogen, C_1 - C_{10} alkyl substituted with 0-3 R^{23} , aryl substituted with 0-3 R^{23} , a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-3 R^{23} , and an electron, provided that when one of R^{19} or R^{20} is an electron, then the other is also an electron;

R^{23} is independently selected at each occurrence from the group: a bond to the targeting moiety, a bond to the linking group, =O, F, Cl, Br, I, $-CF_3$, $-CN$, $-CO_2R^{24}$, $-C(=O)R^{24}$, $-C(=O)N(R^{24})_2$, $-CH_2OR^{24}$, $-OC(=O)R^{24}$, $-OC(=O)OR^{24a}$, $-OR^{24}$, $-OC(=O)N(R^{24})_2$, $-NR^{25}C(=O)R^{24}$, $-NR^{25}C(=O)OR^{24a}$, $-NR^{25}C(=O)N(R^{24})_2$, $-NR^{25}SO_2N(R^{24})_2$, $-NR^{25}SO_2R^{24a}$, $-SO_3H$, $-SO_2R^{24a}$, $-S(=O)R^{24a}$, $-SO_2N(R^{24})_2$, $-N(R^{24})_2$, $-NHC(=S)NHR^{24}$, $=NOR^{18}$, $-C(=O)NHN(R^{18})R^{18a}$, $-OCH_2CO_2H$, and 2-(1-morpholino)ethoxy; and

R^{24} , R^{24a} , and R^{25} are independently selected at each occurrence from the group: a bond to the linking group, H, and C_1 - C_6 alkyl.

22. A compound according to claim 20 wherein the chelator is of the formula:



A¹ is a bond to the linking group;

A², A⁴, and A⁶ are each N;

A³, A⁵, A⁷ and A⁸ are each OH;

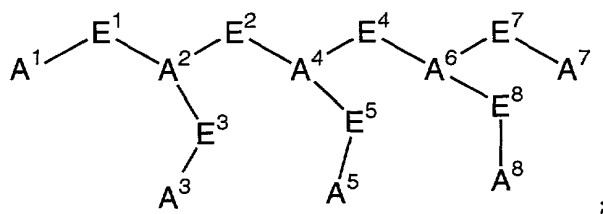
E¹, E², and E⁴ are C₂ alkyl;

E³, E⁵, E⁷, and E⁸ are C₂ alkyl substituted with 0-1 R²³;

R²³ is =O;

23. A compound according to claim 20 wherein the chelator is of the formula:

Ch is



wherein:

A⁵ is a bond to Ln;

A¹, A³, A⁷ and A⁸ are each OH;

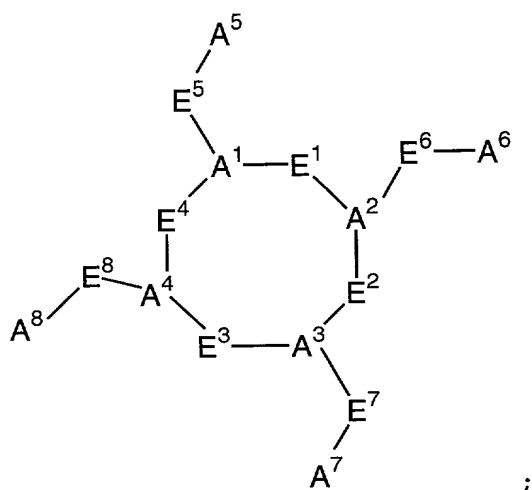
A², A⁴ and A⁶ are each NH;

E¹, E³, E⁵, E⁷, and E⁸ are C₂ alkyl substituted with 0-1 R²³;

E², and E⁴, are C₂ alkyl;

R²³ is =O.

24. A compound according to claim 20 wherein the chelator is of the formula:



A¹, A², A³ and A⁴ are each N;

A⁵, A⁶ and A⁸ are each OH;

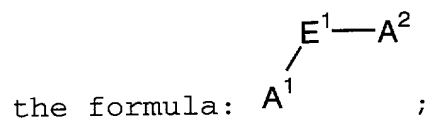
A⁷ is a bond to L_n;

E¹, E², E³, E⁴ are each independently C₂ alkyl; and

E⁵, E⁶, E⁷, E⁸ are each independently C₂ alkyl substituted with 0-1 R²³;

R²³ is =O.

25. A compound according to claim 20 wherein the chelator is of



A¹ is NR²⁶;

R^{26} is a co-ordinate bond to a metal or a hydrazine protecting group;;

E^1 is a bond;

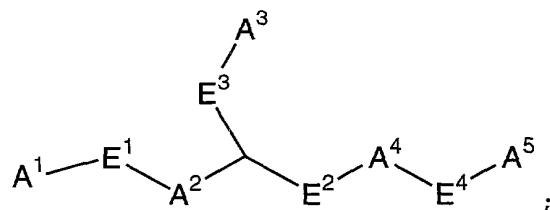
A^2 is NHR^{19} ;

R^{19} is a heterocycle substituted with R^{23} , the heterocycle being selected from pyridine and pyrimidine;

R^{23} is selected from a bond to the linking group, $C(=O)NHR^{24}$ and $C(=O)R^{24}$; and

R^{24} is a bond to the linking group.

26. A compound according to claim 20 wherein the chelator is of the formula:



wherein:

A^1 and A^5 are each $-S(Pg)$;

Pg is a thiol protecting group;

E^1 and E^4 are C_2 alkyl substituted with 0-1 R^{23} ;

R^{23} is $=O$;

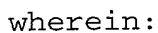
A^2 and A^4 are each $-NH$;

E^2 is CH_2 ;

E^3 is C_{1-3} alkyl substituted with 0-1 R^{23} ;

A^3 is a bond to Ln .

27. A compound according to claim 20 wherein the chelator is of the formula:



E^1 is C_1 alkyl substituted by R^{23} ;

E^2 is C_2 alkyl substituted with 0-1R²³;

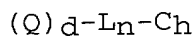
E^3 is C_1 alkyl;

E⁴ and E⁶ are each independently C₁₋₁₆ alkyl substituted with 0-1R²³;

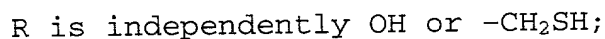
R^{21} is $-OH$; and

$$R^{23} \text{ is } = 0.$$

28. A compound of claim 1 having the formula:



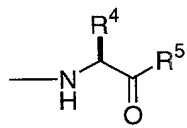
wherein, Q is a compound of Formulae (Ia) or (Ib):



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R² is independently C₁-20 alkyl;

X is independently C=O or SO₂, provided when X is C=O, R³ is



, and when X is SO₂, R³ is independently selected from the group: aryl substituted with 0-2 R⁶, and heterocycle substituted with 0-2 R⁶;

R⁴ is independently selected at each occurrence from the group: C₁-6 alkyl, phenyl, and benzyl;

R⁵ is independently at each occurrence from the group: NH(C₁-6 alkyl), NH-phenyl, and NH-heterocycle; wherein said alkyl, phenyl and heterocycle groups are optionally substituted with a bond to L_n;

R⁶ is independently aryloxy substituted with 0-3 R⁷;

R⁷ is independently halogen or methoxy;

or alternatively,

R¹ and R⁴ may be taken together to form a bridging group of the formula -(CH₂)₃-O-phenyl-CH₂-, optionally substituted with a bond to L_n;

or alternatively,

R¹ and R² may be taken together to form a bridging group of the formula -(CH₂)₃-NH-, optionally substituted with a bond to L_n; or

R¹ and R² taken together with the nitrogen and carbon atom through which they are attached form a C₅₋₇ atom saturated ring system substituted with one or more substituents selected from the group consisting of: a bond to L_n, a bond to Ch, and -C(=O)-NR²⁹R³⁰;

R⁸ is independently at each occurrence OH or phenyl, optionally substituted with a bond to L_n, provided that when R⁸ is phenyl, R¹⁰ is -C(=O)-CR¹²-NH-CH(CH₃)-COOH;

R⁹ and R^{9'} are independently H, C₁₋₆ alkyl optionally substituted with a bond to L_n, or are taken together with the carbon atom to which they are attached to form a 5-7 atom saturated, partially unsaturated or aromatic ring system containing 0-3 heteroatoms selected from O, N, SO₂ and S, said ring system substituted with R⁶ and optionally substituted with a bond to L_n;

R¹⁰ and R¹¹ are independently H, or C₁₋₆ alkyl optionally substituted with a bond to L_n, or are taken together with the nitrogen atom to which they are attached to form a 5-7 atom saturated, partially unsaturated or aromatic ring system containing 0-3 heteroatoms selected from O, N, SO₂ and S, said ring system optionally substituted with 0-3 R²⁷ or a bond to L_n;

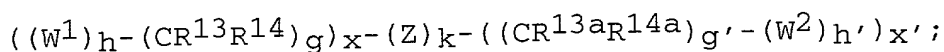
or alternatively,

R⁹ and R¹⁰ are taken together with the carbon atom to which they are attached to form a 5-7 atom saturated, partially unsaturated or aromatic ring system containing 0-3 heteroatoms selected from O, N, SO₂ and S, said ring system optionally substituted with a bond to L_n;

R¹² is independently C₁₋₂₀ alkyl;

d is selected from 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;

L_n is a linking group having the formula:



W¹ and W² are independently selected at each occurrence from the group: O, S, NH, NHC(=O), C(=O)NH, NR¹⁵C(=O), C(=O)NR¹⁵, C(=O), C(=O)O, OC(=O), NHC(=S)NH, NHC(=O)NH, SO₂, SO₂NH, - (OCH₂CH₂)₇₆₋₈₄, (OCH₂CH₂)_s, (CH₂CH₂O)_{s'}, (OCH₂CH₂CH₂)_{s''}, (CH₂CH₂CH₂O)_t, and (aa)_{t'};

aa is independently at each occurrence an amino acid;

Z is selected from the group: aryl substituted with 0-3 R¹⁶, C₃₋₁₀ cycloalkyl substituted with 0-3 R¹⁶, and a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-3 R¹⁶;

R¹³, R^{13a}, R¹⁴, R^{14a}, and R¹⁵ are independently selected at each occurrence from the group: H, =O, COOH, SO₃H, PO₃H, C₁₋₅ alkyl substituted with 0-3 R¹⁶, aryl substituted with 0-3 R¹⁶, benzyl substituted with 0-3 R¹⁶, and C₁₋₅ alkoxy substituted with 0-3 R¹⁶, NHC(=O)R¹⁷, C(=O)NHR¹⁷, NHC(=O)NHR¹⁷, NHR¹⁷, R¹⁷, and a bond to C_H;

R¹⁶ is independently selected at each occurrence from the group: a bond to C_H, COOR¹⁷, C(=O)NHR¹⁷, NHC(=O)R¹⁷, OH, NHR¹⁷, SO₃H, PO₃H, -OPO₃H₂, -OSO₃H, aryl substituted with 0-3 R¹⁷,

C₁₋₅ alkyl substituted with 0-1 R¹⁸, C₁₋₅ alkoxy substituted with 0-1 R¹⁸, and a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-3 R¹⁷;

R¹⁷ is independently selected at each occurrence from the group:

H, alkyl substituted with 0-1 R¹⁸, aryl substituted with 0-1 R¹⁸, a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-1 R¹⁸, C₃₋₁₀ cycloalkyl substituted with 0-1 R¹⁸, polyalkylene glycol substituted with 0-1 R¹⁸, carbohydrate substituted with 0-1 R¹⁸, cyclodextrin substituted with 0-1 R¹⁸, amino acid substituted with 0-1 R¹⁸, polycarboxyalkyl substituted with 0-1 R¹⁸, polyazaalkyl substituted with 0-1 R¹⁸, peptide substituted with 0-1 R¹⁸, wherein the peptide is comprised of 2-10 amino acids, 3,6-O-disulfo-B-D-galactopyranosyl, bis(phosphonomethyl)glycine, and a bond to Ch;

R¹⁸ is a bond to Ch;

k is selected from 0, 1, and 2;

h is selected from 0, 1, and 2;

h' is selected from 0, 1, and 2;

g is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;

g' is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;

s is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;

s' is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;

s" is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;

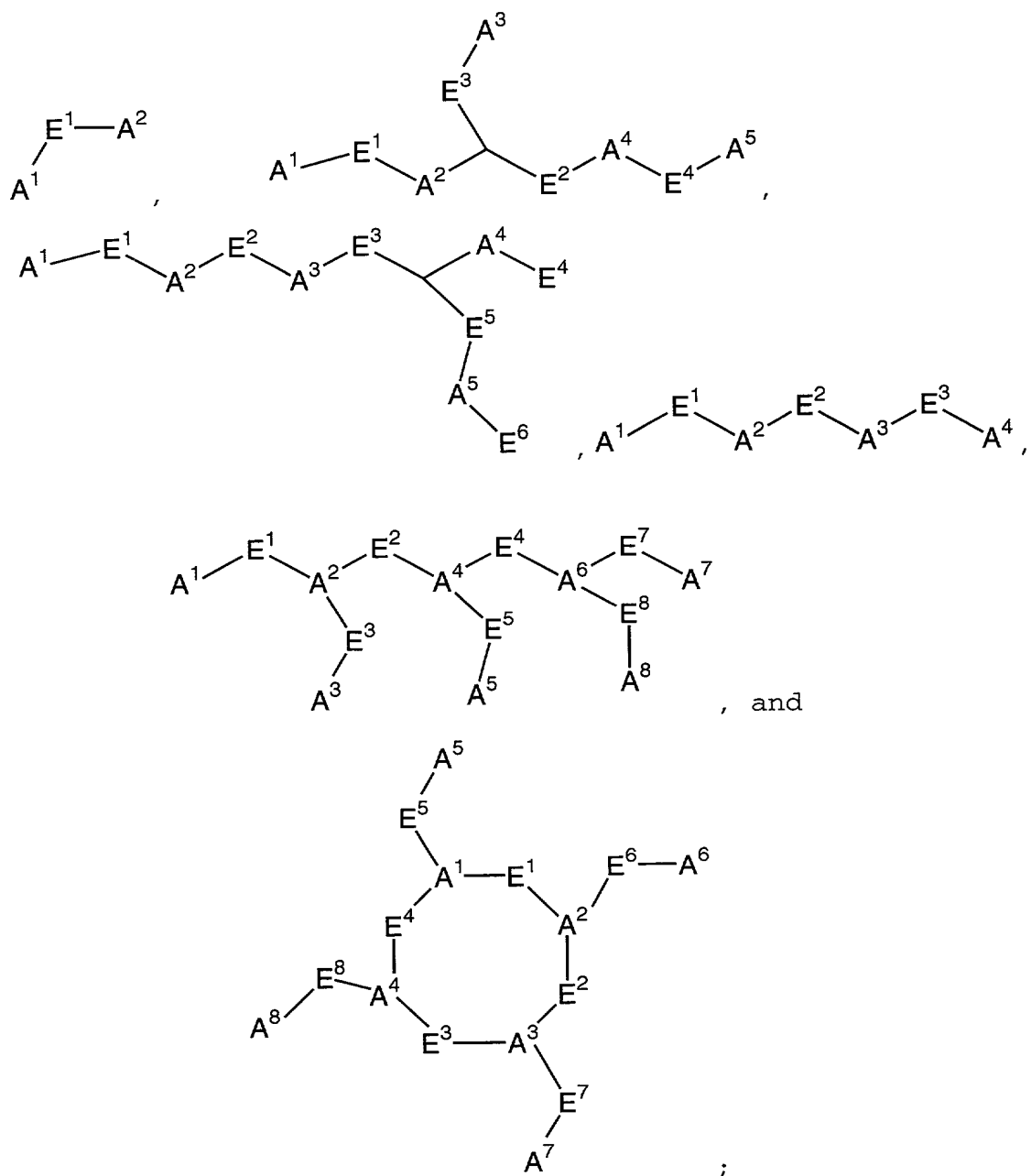
t is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;

t' is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;

x is selected from 0, 1, 2, 3, 4, and 5;

x' is selected from 0, 1, 2, 3, 4, and 5;

Ch is a metal bonding unit having a formula selected from the group:



A¹, A², A³, A⁴, A⁵, A⁶, A⁷, and A⁸ are independently selected at each occurrence from the group: N, NR²⁶, NR¹⁹, NR¹⁹R²⁰, S, SH, -S(Pg), O, OH, PR¹⁹, PR¹⁹R²⁰, -O-P(O)(R²¹)-O-,

$P(O)R^{21}R^{22}$, a bond to the targeting moiety and a bond to the linking group;

P_g is a thiol protecting group;

E^1 , E^2 , E^3 , E^4 , E^5 , E^6 , E^7 , and E^8 are independently a bond, CH, or a spacer group independently selected at each occurrence from the group: C_1 - C_{16} alkyl substituted with 0-3 R^{23} , aryl substituted with 0-3 R^{23} , C_3 -10 cycloalkyl substituted with 0-3 R^{23} , heterocyclo- C_1 -10 alkyl substituted with 0-3 R^{23} , wherein the heterocyclo group is a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O, C_6 -10 aryl- C_1 -10 alkyl substituted with 0-3 R^{23} , C_1 -10 alkyl- C_6 -10 aryl-substituted with 0-3 R^{23} , and a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-3 R^{23} ;

R^{19} and R^{20} are each independently selected from the group: a bond to the linking group, a bond to the targeting moiety, hydrogen, C_1 - C_{10} alkyl substituted with 0-3 R^{23} , aryl substituted with 0-3 R^{23} , C_1 -10 cycloalkyl substituted with 0-3 R^{23} , heterocyclo- C_1 -10 alkyl substituted with 0-3 R^{23} , wherein the heterocyclo group is a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O, C_6 -10 aryl- C_1 -10 alkyl substituted with 0-3 R^{23} , C_1 -10 alkyl- C_6 -10 aryl-substituted with 0-3 R^{23} , a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-3 R^{23} , and an electron, provided that when one of R^{19} or R^{20} is an electron, then the other is also an electron;

R²¹ and R²² are each independently selected from the group: a bond to the linking group, a bond to the targeting moiety, -OH, C₁-C₁₀ alkyl substituted with 0-3 R²³, C₁-C₁₀ alkyl substituted with 0-3 R²³, aryl substituted with 0-3 R²³, C₃-C₁₀ cycloalkyl substituted with 0-3 R²³, heterocyclo-C₁-C₁₀ alkyl substituted with 0-3 R²³, wherein the heterocyclo group is a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O, C₆-C₁₀ aryl-C₁-C₁₀ alkyl substituted with 0-3 R²³, C₁-C₁₀ alkyl-C₆-C₁₀ aryl- substituted with 0-3 R²³, and a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-3 R²³;

R²³ is independently selected at each occurrence from the group: a bond to the linking group, a bond to the targeting moiety, =O, F, Cl, Br, I, -CF₃, -CN, -CO₂R²⁴, -C(=O)R²⁴, -C(=O)N(R²⁴)₂, -CHO, -CH₂OR²⁴, -OC(=O)R²⁴, -OC(=O)OR^{24a}, -OR²⁴, -OC(=O)N(R²⁴)₂, -NR²⁵C(=O)R²⁴, -NR²⁵C(=O)OR^{24a}, -NR²⁵C(=O)N(R²⁴)₂, -NR²⁵SO₂N(R²⁴)₂, -NR²⁵SO₂R^{24a}, -SO₃H, -SO₂R^{24a}, -SR²⁴, -S(=O)R^{24a}, -SO₂N(R²⁴)₂, -N(R²⁴)₂, -NHC(=S)NHR²⁴, =NOR²⁴, NO₂, -C(=O)NHR²⁴, -C(=O)NHN(R²⁴)₂, -OCH₂CO₂H, 2-(1-morpholino)ethoxy, C₁-C₅ alkyl, C₂-C₄ alkenyl, C₃-C₆ cycloalkyl, C₃-C₆ cycloalkylmethyl, C₂-C₆ alkoxyalkyl, aryl substituted with 0-2 R²⁴, and a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O; and wherein at least one of A¹, A², A³, A⁴, A⁵, A⁶, A⁷, A⁸ or R²³ is a bond to the linking group or targeting moiety;

R²⁴, R^{24a}, and R²⁵ are independently selected at each occurrence from the group: a bond to the linking group, a bond to the

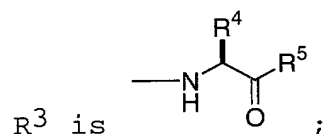
targeting moiety, H, C₁-C₆ alkyl, phenyl, benzyl, C₁-C₆ alkoxy, halide, nitro, cyano, and trifluoromethyl; and
 R²⁶ is a co-ordinate bond to a metal or a hydrazine protecting group; or
 a pharmaceutically acceptable salt thereof.

29. A compound according to claim 28 wherein:

R is -OH;

R² is C₁-6 alkyl;

X is C=O;



R¹ and R⁴ are taken together to form a bridging group of formula
 -(CH₂)₃-O-phenyl-CH₂-;

R⁵ is NH(C₁-6alkyl), substituted with a bond to the linking group or a bond to the chelator.

30. A compound according to claim 28 wherein:

R is -OH;

R⁹ is C₁ alkyl substituted with a bond to Ln;

R¹⁰ and R¹¹ taken together with the nitrogen atom to which they are attached form a 5 atom saturated ring system, said ring system is substituted with 0-3 R²⁷;

R²⁷ is =O, C₁-4 alkyl, or phenyl substituted with R²⁸; and

R²⁸ is a phenoxy group substituted with 0-2 OCH₃ groups.

31. A compound according to claim 28 wherein

R is -OH;

R¹ and R² taken together with the nitrogen and carbon atom through which they are attached form a C₅-7 atom saturated ring system substituted with one or more substituents selected from

the group consisting of: a bond to Ln, a bond to Ch, and $-C(=O)-NR^{29}R^{30}$;

R^{29} and R^{30} taken together with the nitrogen atom through which they are attached form a C5-7 atom saturated ring system substituted with R^{31} ; and

R^{31} is a benzyloxy group substituted with C1-4 alkyl.

32. A compound according to claim 28 wherein

d is selected from 1, 2, 3, 4, and 5;

W is independently selected at each occurrence from the group:

O, NH, $NHC(=O)$, $C(=O)NH$, $NR^{15}C(=O)$, $C(=O)NR^{15}$, $C(=O)$, $C(=O)O$, $OC(=O)$, $NHC(=S)NH$, $NHC(=O)NH$, SO_2 , $(OCH_2CH_2)_s$, $(CH_2CH_2O)_s'$, $(OCH_2CH_2CH_2)_s''$, $(CH_2CH_2CH_2O)_t$, and $(aa)_t'$;

aa is independently at each occurrence an amino acid;

Z is selected from the group: aryl substituted with 0-1 R^{16} , C3-10 cycloalkyl substituted with 0-1 R^{16} , and a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-1 R^{16} ;

R^{13} , R^{13a} , R^{14} , R^{14a} , and R^{15} are independently selected at each occurrence from the group: H, =O, COOH, SO_3H , C1-C5 alkyl substituted with 0-1 R^{16} , aryl substituted with 0-1 R^{16} , benzyl substituted with 0-1 R^{16} , and C1-C5 alkoxy substituted with 0-1 R^{16} , $NHC(=O)R^{17}$, $C(=O)NHR^{17}$, $NHC(=O)NHR^{17}$, NHR^{17} , R^{17} , and a bond to Ch;

k is 0 or 1;

s is selected from 0, 1, 2, 3, 4, and 5;

s' is selected from 0, 1, 2, 3, 4, and 5;

s" is selected from 0, 1, 2, 3, 4, and 5;

t is selected from 0, 1, 2, 3, 4, and 5;

A¹, A², A³, A⁴, A⁵, A⁶, A⁷, and A⁸ are independently selected at each occurrence from the group: NR¹⁹, NR¹⁹R²⁰, S, SH, OH, and a bond to L_n;

E is a bond, CH, or a spacer group independently selected at each occurrence from the group: C₁-C₁₀ alkyl substituted with 0-3 R²³, aryl substituted with 0-3 R²³, C₃-10 cycloalkyl substituted with 0-3 R²³, and a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-3 R²³;

R¹⁹, and R²⁰ are each independently selected from the group: a bond to L_n, hydrogen, C₁-C₁₀ alkyl substituted with 0-3 R²³, aryl substituted with 0-3 R²³, a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-3 R²³, and an electron, provided that when one of R¹⁹ or R²⁰ is an electron, then the other is also an electron;

R²³ is independently selected at each occurrence from the group:
 a bond to L_n, =O, F, Cl, Br, I, -CF₃, -CN, -CO₂R²⁴,
 -C(=O)R²⁴, -C(=O)N(R²⁴)₂, -CH₂OR²⁴, -OC(=O)R²⁴,
 -OC(=O)OR^{24a}, -OR²⁴, -OC(=O)N(R²⁴)₂, -NR²⁵C(=O)R²⁴,
 -NR²⁵C(=O)OR^{24a}, -NR²⁵C(=O)N(R²⁴)₂, -NR²⁵SO₂N(R²⁴)₂,
 -NR²⁵SO₂R^{24a}, -SO₃H, -SO₂R^{24a}, -S(=O)R^{24a}, -SO₂N(R²⁴)₂,

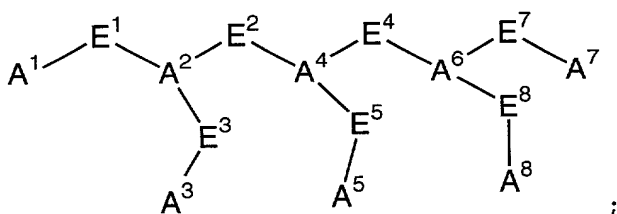
$-\text{N}(\text{R}^{24})_2$, $-\text{NHC}(=\text{S})\text{NHR}^{24}$, $=\text{NOR}^{18}$, $-\text{C}(=\text{O})\text{NHN}^{18}\text{R}^{18a}$,
 $-\text{OCH}_2\text{CO}_2\text{H}$, and 2-(1-morpholino)ethoxy; and

R^{24} , R^{24a} , and R^{25} are independently selected at each occurrence
 from the group: a bond to L_n , H, and $\text{C}_1\text{-C}_6$ alkyl; and

33. A compound according to claim 28 wherein

d is 1,

C_h is



A¹ is a bond to L_n ;

A², A⁴, and A⁶ are each N;

A³, A⁵, A⁷ and A⁸ are each OH;

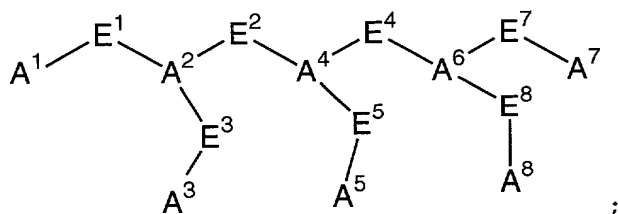
E¹, E², and E⁴ are C_2 alkyl;

E³, E⁵, E⁷, and E⁸ are C_2 alkyl substituted with 0-1 R^{23} ;

R^{23} is =O;

34. A compound according to claim 28 wherein

C_h is



wherein:

A5 is a bond to Ln;

A¹, A³, A⁷ and A⁸ are each OH;

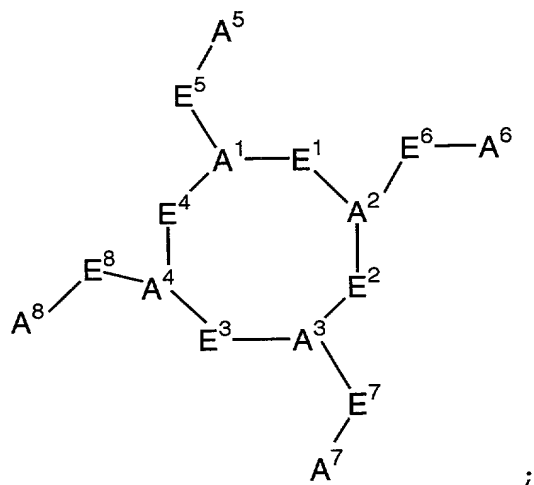
A², A⁴ and A⁶ are each NH;

E¹, E³, E⁵, E⁷, and E⁸ are C₂ alkyl substituted with 0-1 R²³;

E², and E⁴, are C₂ alkyl;

R²³ is =O.

35. A compound according to claim 28 wherein



A¹, A², A³ and A⁴ are each N;

A⁵, A⁶ and A⁸ are each OH;

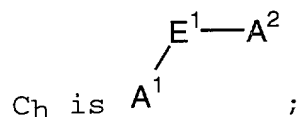
A⁷ is a bond to Ln;

E¹, E², E³, E⁴ are each independently, C₂ alkyl; and

E⁵, E⁶, E⁷, E⁸ are each independently, C₂ alkyl substituted
with 0-1 R²³;

R²³ is =O;

36. A compound according to claim 28 wherein



A¹ is NR²⁶;

R²⁶ is a co-ordinate bond to a metal; or a hydrazine protecting group;

E¹ is a bond;

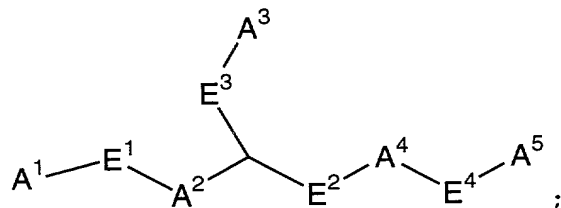
A² is NHR¹⁹;

R¹⁹ is a heterocycle substituted with R²³, the heterocycle being selected from pyridine and pyrimidine;

R²³ is selected from a bond to L_n, C(=O)NHR²⁴ and C(=O)R²⁴; and

R²⁴ is a bond to L_n.

37. A compound according to claim 28 wherein



wherein:

A¹ and A⁵ are each -S(Pg);

Pg is a thiol protecting group;

E¹ and E⁴ are C₂ alkyl substituted with 0-1 R²³;

R²³ is =O;

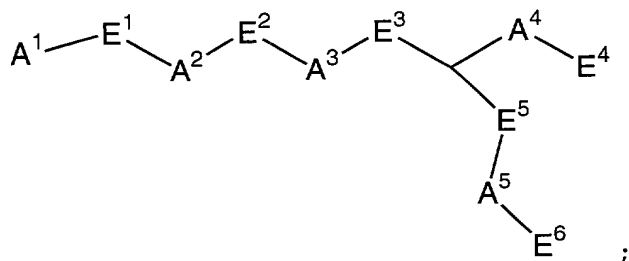
A² and A⁴ are each -NH;

E^2 is CH_2 ;

E^3 is C1-3 alkyl substituted with 0-1 R^{23} ;

A^3 is a bond to Ln.

38. A compound according to claim 28 wherein



wherein:

A^1 is a bond to Ln;

E^1 is C_1 alkyl substituted by R^{23} ;

A^2 is NH;

E^2 is C_2 alkyl substituted with 0-1 R^{23} ;

A^3 is $-O-P(O)(R^{21})-O$;

E^3 is C_1 alkyl;

A^4 and A^5 are each $-O-$;

E^4 and E^6 are each independently C_{1-16} alkyl substituted with 0-1 R^{23} ;

E^5 is C_1 alkyl;

A^5 is $-O-$;

R^{21} is $-OH$; and

R^{23} is $=O$.

39. A compound according to claim 28 wherein

W^1 is $C(=O)NR^{15}$;

h is 1;

g is 3;

R^{13} and R^{14} are independently H;

x is 1;

k is 0;

g' is 0;

h' is 1;

W^2 is NH; and

x' is 1.

40. A compound according to claim 28 wherein

x is 0;

k is 1;

Z is aryl substituted with 0-3 R¹⁶;

g' is 1;

W² is NH;

R^{13a} and R^{14a} are independently H;

h' is 1; and

x' is 1.

41. A compound according to claim 28 wherein

W¹ is C(=O)NR¹⁵;

h is 1;

g is 2;

R¹³ and R¹⁴ are independently H;

x is 1;

k is 0;

g' is 1;

R^{13a} and R^{14a} are independently H; or C1-5 alkyl substituted with 0-3 R¹⁶;

R¹⁶ is SO₃H;

W² is NHC(=O) or NH;

h' is 1; and

x' is 2.

42. A compound according to claim 28 wherein

W¹ is C(=O)NH;

h is 1;

g is 3;

R¹³ and R¹⁴ are independently H;

k is 0;

g' is 0;

x is 1;

W² is -NH(C=O)- or -(OCH₂CH₂)₇₆₋₈₄-;

h' is 2; and

x' is 1.

43. A compound according to claim 28 wherein

x is 0;

k is 0;

g' is 3;

h' is 1;

W² is NH; and

x' is 1.

44. A compound according to claim 28 wherein

x is 0;

Z is aryl substituted with 0-3 R¹⁶;

k is 1;

g' is 1;

R^{13a}R^{14a} are independently H;

W² is NHC(=O) or -(OCH₂CH₂)₇₆₋₈₄-; and

x' is 1.

45. A compound according to claim 28 wherein

W¹ is C=O;

g is 2;

R¹³ and R¹⁴ are independently H;

k is 0;

g' is 0;

h' is 1;

W² is NH; and

x' is 1.

46. A compound according to claim 1 selected from the group consisting of:

2-([5-(3-{2-[(6-Hydroxycarbamoyl-7-isobutyl-8-oxo-2-oxa-9-aza-bicyclo[10.2.2]hexadeca-1(15),12(16),13-triene-10-carbonyl)-amino]-acetylamino}-propylcarbamoyl)-pyridin-2-yl]-hydrazonomethyl)-benzenesulfonic acid;

2-([5-(4-{[(6-Hydroxycarbamoyl-7-isobutyl-8-oxo-2-oxa-9-aza-bicyclo[10.2.2]hexadeca-1(15),12(16),13-triene-10-carbonyl)-amino]-methyl}-benzylcarbamoyl)-pyridin-2-yl]-hydrazonomethyl)-benzenesulfonic acid;

2-[7-({N-[3-(2-{[7-(N-hydroxycarbamoyl)(3S,6R,7S)-4-aza-6-(2-methylpropyl)-11-oxa-5-oxobicyclo[10.2.2]hexadeca-1(15),12(16),13-trien-3-yl]carbonylamino}acetylamino)propyl]carbamoyl)methyl)-1,4,7,10-tetraaza-4,10-bis(carboxymethyl)cyclododecyl]acetic acid;

2-{7-[(N-{[4-({[7-(N-hydroxycarbamoyl)(3S,6R,7S)-4-aza-6-(2-methylpropyl)-11-oxa-5-oxobicyclo[10.2.2]hexadeca-1(15),12(16),13-trien-3-yl]-carbonylamino}methyl)phenyl]methyl}carbamoyl)methyl]-1,4,7,10-tetraaza-4,10-bis(carboxymethyl)cyclododecyl]acetic acid;

2-(7-{[N-(1-{N-[3-(2-{[7-(N-hydroxycarbamoyl)(3S,6R,7S)-4-aza-6-(2-methylpropyl)-11-oxa-5-oxobicyclo[10.2.2]hexadeca-1(15),12(16),13-trien-3-yl]carbonylamino}acetylamino)propyl]carbamoyl}-2-sulfoethyl)carbamoyl)methyl]-1,4,7,10-tetraaza-4,10-bis(carboxymethyl)cyclododecyl]acetic acid;

2-[7-({N-[1-(N-{[4-({[7-(N-hydroxycarbamoyl)(3S,6R,7S)-4-aza-6-(2-methylpropyl)-11-oxa-5-oxobicyclo[10.2.2]hexadeca-1(15),12(16),13-trien-3-yl]-carbonylamino}methyl)phenyl]methyl}carbamoyl)-2-sulfoethyl]carbamoyl)methyl)-1,4,7,10-tetraaza-4,10-bis(carboxymethyl)cyclododecyl]acetic acid;

2-({2-[(N-[3-(2-{[7-(N-hydroxycarbamoyl)(3S,6R,7S)-4-aza-6-(2-methylpropyl)-11-oxa-5-oxobicyclo[10.2.2]hexadeca-1(15),12(16),13-trien-3-yl]carbonylamino}acetylaminopropyl]carbamoyl)methyl](carboxymethyl)amino}ethyl){2-[bis(carboxymethyl)amino]ethyl}amino}acetic acid;

2-[(2-[(N-[4-({[7-(N-hydroxycarbamoyl)(3S,6R,7S)-4-aza-6-(2-methylpropyl)-11-oxa-5-oxobicyclo[10.2.2]hexadeca-1(15),12(16),13-trien-3-yl]-carbonylamino)methyl]phenyl)methyl]carbamoyl)methyl](carboxymethyl)amino}ethyl){2-[bis(carboxymethyl)amino]ethyl}amino}acetic acid;

N-[3-(2-{[7-(N-hydroxycarbamoyl)(3S,6R,7S)-4-aza-6-(2-methylpropyl)-11-oxa-5-oxobicyclo[10.2.2]hexadeca-1(15),12(16),13-trien-3-yl]carbonylamino}acetylaminopropyl]-4,5-bis[2-(ethoxyethylthio)acetylaminopentanamide];

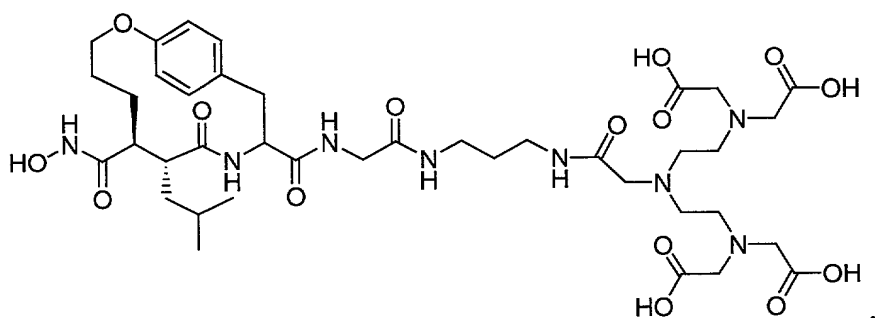
N-{[4-({[7-(N-hydroxycarbamoyl)(3S,6R,7S)-4-aza-6-(2-methylpropyl)-11-oxa-5-oxobicyclo[10.2.2]hexadeca-1(15),12(16),13-trien-3-yl]carbonylamino)methyl]-phenyl)methyl]-4,5-bis[2-(ethoxyethylthio)acetylaminopentanamide];

1-(1,2-Dipalmitoyl-sn-glycero-3-phosphoethanolamino)- α,ω -dicarbonylPEG3400-2-{[7-(N-hydroxycarbamoyl)(3S,6R,7S)-4-aza-6-(2-methylpropyl)-11-oxa-5-oxobicyclo[10.2.2]hexadeca-1(15),12(16),13-trien-3-yl]carbonylamino}-N-(3-aminopropyl)acetamide;

1-(1,2-Dipalmitoyl-sn-glycero-3-phosphoethanolamino)- α,ω -dicarbonylPEG3400-[7-(N-hydroxycarbamoyl)(3S,6R,7S)-4-aza-6-(2-methylpropyl)-11-oxa-5-oxobicyclo[10.2.2]hexadeca-1(15),12(16),13-trien-3-yl]-N-{[4-(aminomethyl)phenyl)methyl]carboxamide conjugate;

2-[2-({5-[N-(5-(N-hydroxycarbamoyl)(5R)-5-{3-[4-(3,4-dimethoxyphenoxy)phenyl]-3-methyl-2-oxopyrrolidinyl}pentyl)carbamoyl](2-pyridyl)}amino)(1Z)-2-azavinyl]benzenesulfonic acid;

2-(2-{[5-(N-{3-[3-(N-hydroxycarbamoyl)(4S)-4-({4-[(4-methylphenyl)methoxy]piperidyl}carbonyl)piperidyl]-3-oxopropyl}carbamoyl)(2-pyridyl)]amino}(1Z)-2-azavinyl)benzenesulfonic acid; and



47. A radiopharmaceutical comprising a compound of claim 1 and a cytotoxic radioisotope which is complexed to the chelator.
48. A radiopharmaceutical comprising a compound of claim 28 and a cytotoxic radioisotope which is complexed to the chelator.
49. A radiopharmaceutical comprising a compound of claim 46 and a cytotoxic radioisotope.
50. A radiopharmaceutical according to claim 20 selected from the group consisting of:
 2-{[5-(3-{2-[(6-Hydroxycarbamoyl-7-isobutyl-8-oxo-2-oxa-9-azabicyclo[10.2.2]hexadeca-1(15),12(16),13-triene-10-carbonyl)-amino]-acetyl-amino}-propylcarbonyl)-pyridin-2-yl]-hydrazonomethyl}-benzenesulfonic acid; and

2-{[5-(4-{[(6-Hydroxycarbamoyl-7-isobutyl-8-oxo-2-oxa-9-azabicyclo[10.2.2]hexadeca-1(15),12(16),13-triene-10-carbonyl)-

amino]-methyl)-benzylcarbamoyl)-pyridin-2-yl]-hydrazonomethyl)-benzenesulfonic acid;

wherein the cytotoxic radioisotope is ^{99m}Tc .

51. A radiopharmaceutical according to claim 47 wherein the cytotoxic radioisotope is selected from the group consisting of beta particle emitters, alpha particle emitters, and Auger electron emitters.

52. A radiopharmaceutical according to claim 47 wherein the cytotoxic radioisotope is selected from the group consisting of: ^{186}Re , ^{188}Re , ^{153}Sm , ^{166}Ho , ^{177}Lu , ^{149}Pm , ^{90}Y , ^{212}Bi , ^{103}Pd , ^{109}Pd , ^{159}Gd , ^{140}La , ^{198}Au , ^{199}Au , ^{169}Yb , ^{175}Yb , ^{165}Dy , ^{166}Dy , ^{67}Cu , ^{105}Rh , ^{111}Ag , and ^{192}Ir .

53. A radiopharmaceutical according to claim 47 wherein the cytotoxic radioisotope is selected from the group consisting of: ^{186}Re , ^{188}Re , ^{153}Sm , ^{166}Ho , ^{177}Lu , ^{149}Pm , ^{90}Y , ^{212}Bi , ^{103}Pd , and ^{105}Rh .

54. A radiopharmaceutical according to claim 47 wherein the cytotoxic radioisotope is selected from the group consisting of: ^{186}Re , ^{188}Re , ^{153}Sm , ^{166}Ho , ^{177}Lu , ^{149}Pm , ^{90}Y , and ^{212}Bi .

55. A composition comprising a compound of claim 1, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier.

56. A radiopharmaceutical composition comprising a compound of claim 47, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier.

57. A radiopharmaceutical composition according to claim 56, further comprising at least one agent selected from the group

consisting of a chemotherapeutic agent and a radiosensitizer agent, or a pharmaceutically acceptable salt thereof.

58. A radiopharmaceutical composition according to claim 57, wherein the chemotherapeutic agent is selected from the group consisting of mitomycin, tretinoin, ribomustin, gemcitabine, vincristine, etoposide, cladribine, mitobronitol, methotrexate, doxorubicin, carboquone, pentostatin, nitracrine, zinostatin, cetorelix, letrozole, raltitrexed, daunorubicin, fadrozole, fotemustine, thymalfasin, sobuzoxane, nedaplatin, cytarabine, bicalutamide, vinorelbine, vesnarinone, aminoglutethimide, amsacrine, proglumide, elliptinium acetate, ketanserin, doxifluridine, etretinate, isotretinoin, streptozocin, nimustine, vindesine, flutamide, drogenil, butocin, carmofur, razoxane, sizofilan, carboplatin, mitolactol, tegafur, ifosfamide, prednimustine, picibanil, levamisole, teniposide, improsulfan, enocitabine, lisuride, oxymetholone, tamoxifen, progesterone, mepitiostane, epitio stanol, formestane, interferon-alpha, interferon-2 alpha, interferon-beta, interferon-gamma, colony stimulating factor-1, colony stimulating factor-2, denileukin diftitox, interleukin-2, and leutinizing hormone releasing factor.

59. A radiopharmaceutical composition according to claim 57, wherein radiosensitizer agent is selected from the group consisting of 2-(3-nitro-1,2,4-triazol-1-yl)-N-(2-methoxyethyl)acetamide, N-(3-nitro-4-quinolinyl)-4-morpholinecarboxamidine, 3-amino-1,2,4-benzotriazine-1,4-dioxide, N-(2-hydroxyethyl)-2-nitroimidazole-1-acetamide, 1-(2-nitroimidazol-1-yl)-3-(1-piperidinyl)-2-propanol, and 1-(2-nitro-1-imidazolyl)-3-(1-aziridino)-2-propanol.

60. A kit comprising a compound of Claim 1, or a pharmaceutically acceptable salt form thereof and a pharmaceutically acceptable carrier.

61. A radiopharmaceutical kit comprising a compound of Claim 47, or a pharmaceutically acceptable salt form thereof and a pharmaceutically acceptable carrier.
62. A kit of Claim 60 further comprising a stabilizer.
63. A radiopharmaceutical kit according to Claim 61, wherein the radioisotope is ^{186}Re or ^{188}Re and the kit further comprises one or more ancillary ligands and a reducing agent.
64. A radiopharmaceutical kit according to Claim 63, wherein the ancillary ligands are tricine and a phosphine.
65. A kit according to claim 60, further comprising and at least one agent selected from the group consisting of a chemotherapeutic agent and a radiosensitizer agent, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier.
66. A kit according to Claim 65, wherein the chemotherapeutic agent is selected from the group consisting of mitomycin, tretinoin, ribomustin, gemcitabine, vincristine, etoposide, cladribine, mitobronitol, methotrexate, doxorubicin, carboquone, pentostatin, nitracrine, zinostatin, cetorelix, letrozole, raltitrexed, daunorubicin, fadrozole, fotemustine, thymalfasin, sobuzoxane, nedaplatin, cytarabine, bicalutamide, vinorelbine, vesnarinone, aminoglutethimide, amsacrine, proglumide, elliptinium acetate, ketanserin, doxifluridine, etretinate, isotretinoin, streptozocin, nimustine, vindesine, flutamide, drogenil, butocin, carmofur, razoxane, sizofilan, carboplatin, mitolactol, tegafur, ifosfamide, prednimustine, picibanil, levamisole, teniposide, improsulfan, enocitabine, lisuride, oxymetholone, tamoxifen, progesterone, mepitiostane, epitiostanol, formestane, interferon-alpha, interferon-2 alpha, interferon-beta, interferon-gamma, colony stimulating factor-1,

colony stimulating factor-2, denileukin diftitox, interleukin-2, and leutinizing hormone releasing factor.

67. A kit according to Claim 65, wherein radiosensitizer agent is selected from the group consisting of 2-(3-nitro-1,2,4-triazol-1-yl)-N-(2-methoxyethyl)acetamide, N-(3-nitro-4-quinoliny1)-4-morpholinecarboxamidine, 3-amino-1,2,4-benzotriazine-1,4-dioxide, N-(2-hydroxyethyl)-2-nitroimidazole-1-acetamide, 1-(2-nitroimidazol-1-yl)-3-(1-piperidinyl)-2-propanol, and 1-(2-nitro-1-imidazolyl)-3-(1-aziridino)-2-propanol.

68. A method of treating a pathological disorder mediated by a matrix metalloproteinase in a patient which comprises administering to a patient in need thereof a therapeutically effective amount of a radiopharmaceutical according to claim 47. and a pharmaceutically acceptable carrier.

69. A method of claim 68, wherein the disorder is selected from the group consisting of atherosclerosis, restenosis, angiogenesis, tumor metastasis, tumor growth, osteoarthritis, and rheumatoid arthritis.

70. A method of claim 68, wherein the disorder is age related macular degeneration, diabetic retinopathy, proliferative vitreoretinopathy, retinopathy of prematurity, ocular tumors, ocular angiogenesis/neovascularization and corneal graft rejection.

71. A method of claim 68, wherein the disorder is cancer selected from the group consisting of prostate, breast, colon, lung melanoma and lymph cancer.

72. A method of inhibiting proliferation of cancer cells, comprising contacting the cancer cells with a proliferation-inhibitory amount of a radiopharmaceutical of claim 47.

73. A method of claim 68, wherein the matrix metalloproteinase is selected from the group consisting of: MMP-1, MMP-2, MMP-3, MMP-9, and MMP-14.

74. A method of claim 68 wherein the matrix metalloproteinase is selected from the group consisting of: MMP-2, MMP-9, and MMP-14.

75. A method of treating cancer in a patient comprising: administering to a patient in need thereof a therapeutic radiopharmaceutical of claim 47 or a pharmaceutically acceptable salt thereof, and at least one agent selected from the group consisting of a chemotherapeutic agent and a radiosensitizer agent, or a pharmaceutically acceptable salt thereof.

76. A method according to claim 75 wherein the chemotherapeutic agent is selected from the group consisting of mitomycin, tretinoin, ribomustin, gemcitabine, vincristine, etoposide, cladribine, mitobronitol, methotrexate, doxorubicin, carboquone, pentostatin, nitracrine, zinostatin, cetorelix, letrozole, raltitrexed, daunorubicin, fadrozole, fotemustine, thymalfasin, sobuzoxane, nedaplatin, cytarabine, bicalutamide, vinorelbine, vesnarinone, aminoglutethimide, amsacrine, proglumide, elliptinium acetate, ketanserin, doxifluridine, etretinate, isotretinoin, streptozocin, nimustine, vindesine, flutamide, drogenil, butocin, carmofur, razoxane, sizofilan, carboplatin, mitolactol, tegafur, ifosfamide, prednimustine, picibanil, levamisole, teniposide, improsulfan, enocitabine, lisuride, oxymetholone, tamoxifen, progesterone, mepitiostane, epitiostanol, formestane, interferon-alpha, interferon-2 alpha, interferon-beta, interferon-gamma, colony stimulating factor-1, colony stimulating factor-2, denileukin diftitox, interleukin-2, and leutinizing hormone releasing factor.

77. A method according to claim 75 wherein the radiosensitizer agent is selected from the group consisting of 2-(3-nitro-1,2,4-triazol-1-yl)-N-(2-methoxyethyl)acetamide, N-(3-nitro-4-quinoliny)-4-morpholinecarboxamidine, 3-amino-1,2,4-benzotriazine-1,4-dioxide, N-(2-hydroxyethyl)-2-nitroimidazole-1-acetamide, 1-(2-nitroimidazol-1-yl)-3-(1-piperidinyl)-2-propanol, and 1-(2-nitro-1-imidazolyl)-3-(1-aziridino)-2-propanol.

78. A process for the preparation of a radiopharmaceutical, said process comprising generating a macrostructure from a plurality of molecular components wherein the plurality of components includes a compound of claim 1 and a cytotoxic radioisotope.

79. A compound as disclosed in any of the examples described herein.